



## SEQUENCE LISTING

<110> Martin, John Francis  
Yla-Herttuala, Seppo  
Barker, Stephen George Edward

<120> Therapeutic Use of an Agent That Stimulates NO or Prostacyclin Production and Delivery Device

<130> GJE-30

<140> US 09/297,486  
<141> 1999-04-30

<150> PCT/GB97/03015  
<151> 1997-11-03

<150> GB 9622852.3  
<151> 1996-11-01

<150> GB 9709494.0  
<151> 1997-05-09

<150> GB 9717791.9  
<151> 1997-08-21

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48

tac ctc cac cat gcc aag tgg tcc cag gct gca ccc atg gca gaa gga  
Tyr Leu His His Ala Lys Trp Ser Gln Ala Ala Pro Met Ala Glu Gly  
20 25 30

96

gga ggg cag aat cat cac gaa gtg gtg aag ttc atg gat gtc tat cag  
Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln  
35 40 45

144

cgc agc tac tgc cat cca atc gag acc ctg gtg gac atc ttc cag gag  
Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu  
50 55 60

192

tac cct gat gag atc gag tac atc ttc aag cca tcc tgt gtg ccg ctg	240
Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu	
65 70 75 80	
atg cga tgc ggg ggc tgc tgc aat gac gag ggc ctg gag tgt gtg ccc	288
Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro	
85 90 95	
act gag gag tcc aac atc acc atg cag att atg cgg atc aaa cct cac	336
Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His	
100 105 110	
caa ggc cag cac ata gga gag atg agc ttc cta cag cac aac aaa tgt	384
Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys	
115 120 125	
gaa tgc aga cca aag aaa gat aga gca aga caa gaa aaa tgt gac aag	432
Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Lys Cys Asp Lys	
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Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln	
35 40 45	
Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu	
50 55 60	
Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu	
65 70 75 80	
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85 90 95	
Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His	
100 105 110	
Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys	
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Pro Arg Arg  
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tac ctc cac cat gcc aag tgg tcc cag gct gca ccc atg gca gaa gga	96
Tyr Leu His His Ala Lys Trp Ser Gln Ala Ala Pro Met Ala Glu Gly	
20 25 30	
gga ggg cag aat cat cac gaa gtg gtg aag ttc atg gat gtc tat cag	144
Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln	
35 40 45	
cgc agc tac tgc cat cca atc gag acc ctg gtg gac atc ttc cag gag	192
Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu	
50 55 60	
tac cct gat gag atc gag tac atc ttc aag cca tcc tgt gtg ccc ctg	240
Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu	
65 70 75 80	
atg cga tgc ggg ggc tgc tgc aat gac gag ggc ctg gag tgt gtg ccc	288
Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro	
85 90 95	
act gag gag tcc aac atc acc atg cag att atg cgg atc aaa cct cac	336
Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His	
100 105 110	
caa ggc cag cac ata gga gag atg agc ttc cta cag cac aac aaa tgt	384
Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys	
115 120 125	
gaa tgc aga cca aag aaa gat aga gca aga caa gaa aaa ccc tgt ggg	432
Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Lys Pro Cys Gly	
130 135 140	

cct tgc tca gag cgg aga aag cat ttg ttt gta caa gat ccg cag acg	480
Pro Cys Ser Glu Arg Arg Lys His Leu Phe Val Gln Asp Pro Gln Thr	
145 150 155 160	
tgt aaa tgt tcc tgc aaa aac aca gac tcg cgt tgc aag gcg agg cag	528
Cys Lys Cys Ser Cys Lys Asn Thr Asp Ser Arg Cys Lys Ala Arg Gln	
165 170 175	
ctt gag tta aac gaa cgt act tgc aga tgt gac aag ccg agg cgg	573
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Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln	
35 40 45	
Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu	
50 55 60	
Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu	
65 70 75 80	
Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro	
85 90 95	
Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His	
100 105 110	
Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys	
115 120 125	
Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Lys Pro Cys Gly	
130 135 140	
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tac ctc cac cat gcc aag tgg tcc cag gct gca ccc atg gca gaa gga	96
Tyr Leu His His Ala Lys Trp Ser Gln Ala Ala Pro Met Ala Glu Gly	
20 25 30	
gga ggg cag aat cat cac gaa gtg gtg aag ttc atg gat gtc tat cag	144
Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln	
35 40 45	
cgc agc tac tgc cat cca atc gag acc ctg gtg gac atc ttc cag gag	192
Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu	
50 55 60	
tac cct gat gag atc gag tac atc ttc aag cca tcc tgt gtg ccg ctg	240
Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu	
65 70 75 80	
atg cga tgc ggg ggc tgc tgc aat gac gag ggc ctg gag tgt gtg ccc	288
Met Arg Cys Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro	
85 90 95	
act gag gag tcc aac atc acc atg cag att atg cgg atc aaa cct cac	336
Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His	
100 105 110	
caa ggc cag cac ata gga gag atg agc ttc cta cag cac aac aaa tgt	384
Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys	
115 120 125	
gaa tgc aga cca aag aaa gat aga gca aga caa gaa aaa aaa tca gtt	432
Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Lys Lys Ser Val	
130 135 140	
cga gga aag gga aag ggg caa aaa cga aag cgc aag aaa tcc cgg tat	480
Arg Gly Lys Gly Lys Gly Gln Lys Arg Lys Arg Lys Lys Ser Arg Tyr	
145 150 155 160	
aag tcc tgg agc gtg ccc tgt ggg cct tgc tca gag cgg aga aag cat	528
Lys Ser Trp Ser Val Pro Cys Gly Pro Cys Ser Glu Arg Arg Lys His	
165 170 175	

ttg ttt gta caa gat ccg cag acg tgt aaa tgt tcc tgc aaa aac aca	576
Leu Phe Val Gln Asp Pro Gln Thr Cys Lys Cys Ser Cys Lys Asn Thr	
180 185 190	
gac tcg cgt tgc aag gcg agg cag ctt gag tta aac gaa cgt act tgc	624
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35 40 45	
Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu	
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Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu	
65 70 75 80	
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85 90 95	
Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His	
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130 135 140	
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145 150 155 160	
Lys Ser Trp Ser Val Pro Cys Gly Pro Cys Ser Glu Arg Arg Lys His	
165 170 175	
Leu Phe Val Gln Asp Pro Gln Thr Cys Lys Cys Ser Cys Lys Asn Thr	
180 185 190	

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Arg Cys Asp Lys Pro Arg Arg  
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 Tyr Leu His His Ala Lys Trp Ser Gln Ala Ala Pro Met Ala Glu Gly  
 20 25 30

gga ggg cag aat cat cac gaa gtg gtg aag ttc atg gat gtc tat cag 144  
 Gly Gly Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln  
 35 40 45

cgc agc tac tgc cat cca atc gag acc ctg gtg gac atc ttc cag gag 192  
 Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu  
 50 55 60

tac cct gat gag atc gag tac atc ttc aag cca tcc tgt gtg ccg ctg 240  
 Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu  
 65 70 75 80

atg cga tgc ggg ggc tgc aat gac gag ggc ctg gag tgt gtg ccc 288  
 Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro  
 85 90 95

act gag gag tcc aac atc acc atg cag att atg cgg atc aaa cct cac 336  
 Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His  
 100 105 110

caa ggc cag cac ata gga gag atg agc ttc cta cag cac aac aaa tgt 384  
 Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys  
 115 120 125

gaa tgc aga cca aag aaa gat aga gca aga caa gaa aaa aaa tca gtt 432  
 Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Lys Lys Ser Val  
 130 135 140

cga gga aag gga aag ggg caa aaa cga aag cgc aag aaa tcc cgg tat	480
Arg Gly Lys Gly Lys Gly Gln Lys Arg Lys Arg Lys Ser Arg Tyr	
145 150 155 160	
aag tcc tgg agc gtg tac gtt ggt gcc cgc tgc tgt cta atg ccc tgg	528
Lys Ser Trp Ser Val Tyr Val Gly Ala Arg Cys Cys Leu Met Pro Trp	
165 170 175	
agc ctc cct ggc ccc cat ccc tgt ggg cct tgc tca gag cgg aga aag	576
Ser Leu Pro Gly Pro His Pro Cys Gly Pro Cys Ser Glu Arg Arg Lys	
180 185 190	
cat ttg ttt gta caa gat ccg cag acg tgt aaa tgt tcc tgc aaa aac	624
His Leu Phe Val Gln Asp Pro Gln Thr Cys Lys Cys Ser Cys Lys Asn	
195 200 205	
aca gac tcg cgt tgc aag gcg agg cag ctt gag tta aac gaa cgt act	672
Thr Asp Ser Arg Cys Lys Ala Arg Gln Leu Glu Leu Asn Glu Arg Thr	
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Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu	
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Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu	
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Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro	
85 90 95	
Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His	
100 105 110	
Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys	
115 120 125	

Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Lys Lys Ser Val  
130 135 140

Arg Gly Lys Gly Lys Gly Gln Lys Arg Lys Arg Lys Lys Ser Arg Tyr  
145 150 155 160

Lys Ser Trp Ser Val Tyr Val Gly Ala Arg Cys Cys Leu Met Pro Trp  
165 170 175

Ser Leu Pro Gly Pro His Pro Cys Gly Pro Cys Ser Glu Arg Arg Lys  
180 185 190

His Leu Phe Val Gln Asp Pro Gln Thr Cys Lys Cys Ser Cys Lys Asn  
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210 215 220

Cys Arg Cys Asp Lys Pro Arg Arg  
225 230

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